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Pesticide Fact Sheet Number 73: Lindane

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This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

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Office of Pesticide Programs (TS-768C)
Washington, DC 20460

EPA

Pesticide Fact Sheet

Name of Chemical: LINDANE
REGISTRATION STANDARD
Reason for Issuance:
Date Issued: Sept. 30, 1985
Fact Sheet Number: 73

1. Description of Chemical

Generic Name: Gamma Isomer of 1,2,3,4,5,6-hexachloro-cyclohexane
Common Name: Lindane
Trade Names: Exagamma, Forlin, Gallogamma, Gammaphex, Gammex, Gexane, Grammapoz, Grammexane, Inexit, Kwell, Lindafor, Lindagrain, Lindagram, Lindagranox, Lindalo, Lindamul, Lindapoudre, Lindaterra, Lindex, Lindust, Lintox, Novigram, and Silvanol
EPA Shaughnessy Code: 009001
Chemical Abstracts Service (CA) Number: 58-89-9
Year of Initial Registration: 1950
Pesticide Type: insecticide/acaracide
Chemical Family: chlorinated hydrocarbon
U.S. Producer: None
Foreign Producers: Celamerck GmbH KG
Ingelheim, Federal Republic of Germany
Rhone Poulenc Phytosanitaire
Lyon, France
Mitsui, Inc.
Fukuoka, Japan
Tianjin Interntl. Trust & Investment Corp.
Tianjin, China

2. USE PATTERNS AND FORMULATIONS

Application sites: field and vegetable crops (including seed treatment) and non-food crops (ornamentals and tobacco), greenhouse food crops (vegetables) and non-food crops (ornamentals), forestry (including Christmas tree plantations), domestic outdoor and indoor (pets and household), commercial indoor (food/feed storage areas and containers), animal premises (including manure), wood or wooden structures, and human skin/clothing (military use only).

Percent of lindane used on various crops/sites:

Hardwood Lumber	19%
Seed Treatment	48%
Forestry	<1%
Livestock	20%
Pineapple	2%
Ornamentals	2%
Pecans	3%
Pets	3%
Structures	<1%
Household	1%
Cucurbits	1%

Types and methods of applications: dip tank solution (livestock, lumber, and pets), as a livestock spray, by ground equipment delivering a ground or foliar spray or dust, by soil incorporation, by soil injection in combination with a fumigant (for the pineapple use only), as a smoke (for greenhouse fumigation only), as a dust for human skin/clothing (military use only).

Application rates: ranged from 0.25 to 2.25 oz/100 lb of seed for seed treatment; 0.1 to 2.06 lb/A for foliar and soil treatment; 0.8 to 1.5 oz/50,000 ft^3 of greenhouse; 0.006 to 0.11 lb/gal for bark; 0.023 to 3% sprays, dips, and dusts for indoor and animal treatment; <0.01 lb/1,000 ft^2 for animal premises; <4 lb/1000 ft^2 (14.64% solutions for wood and wooden structures; and 1% dust for human skin/clothing treatment (military use only).

Types of formulations: 0.27%-11.2% impregnated formulations, 0.5-75% Dusts, 3%-73% wettable powders, 0.5-25% liquids, 0.25-3% pressurized liquids, 1-4% flowable concentrates, 0.45-40% emulsifiable concentrates,

3. SCIENCE FINDINGS

Summary Science Statement: Lindane is a chlorinated hydrocarbon of moderate mammalian acute toxicity. Lindane has been shown to be oncogenic in mice but it is not genotoxic. The Agency has concluded that lindane is a possible human carcinogen. The Agency is requiring that another rat chronic/oncogenicity bioassay be performed. Lindane has been associated with possible induction of blood dyscrasias (aplastic anemia). The Agency is requiring a laboratory animal study to permit assessment of lindane's potential to cause blood dyscrasias. Other toxicology studies demonstrate systemic toxicity, targeting the liver and kidney. Lindane's behavior in the environment is not well defined. The Agency is requiring a full complement of environmental fate studies. Lindane is slightly to moderately toxic to birds and highly toxic to some aquatic organisms. Lindane is highly toxic to honeybees and certain beneficial parasites and predacious insects. Additional studies on the ecological effects of lindane are required.

Chemical Characteristics

Technical lindane is a white crystalline solid.
Its melting point is 112° - 113°C.
It is soluble in most organic solvents and is relatively insoluble in water.
Lindane is stable to light, heat, air and strong acids, but decomposes to trichlorobenzenes and HCL in alkali.

Toxicology Characteristics

Acute Oral: 88 mg/kg, Toxicity Category II
Acute Dermal: 300 mg/kg Toxicity Category II
Acute Inhalation: Data gap
Primary Eye Irritation: Data gap
Primary Skin Irritation: Irritant Toxicity Category I
Skin Sensitization: Data gap
Major Routes of Exposure: Human exposure from lindane is greatest during mixing, loading, and application. Dermal, ocular, and inhalation exposures to workers may occur during application. Exposure can be reduced by the use of approved respirators, protective clothing, and goggles.
Oncogenicity: A two-year mouse oncogenicity study demonstrated increased incidences of liver tumors (male & female) when dosed at 400 ppm. An 80-week mouse feeding study demonstrated increased incidences of liver tumors at the 80 ppm level but not at the 160 ppm level. Two subchronic studies provide supportive evidence of oncogenicity. The mouse studies were referred to the Agency's Carcinogen Assessment Group (CAG) for evaluation. Based on the weight of the evidence, CAG classifed lindane in the range B2-C. OPP believes that the classification C is appropriate at this time and, therefore, will regulate lindane as a class C carcinogen, pending receipt of the required rat oncogenicity study.
Metabolism: Lindane does not appear to bioaccumulate in tissues.
Teratology: Teratology studies in the rat, rabbit, and mouse were negative for teratogenic effects.
Reproduction: A 3 generation rat reproduction study was negative at 100 ppm.
Mutagenicity: Available data show lindane to be negative for gene mutation in bacterial Ames assays, host mediated, and dominant lethal assays. Lindane has been reported as negative in other in vitro assays for DNA damage/repair in bacteria, rat and mouse hepatocytes, and mammalian cell transformation assays.

Physiological and Biochemical Characteristics

Mechanism of pesticidal action: Lindane acts in the nervous system through unknown mechanisms.
Metabolism and persistence in plants and animals: The metabolism of lindane in plants and livestock animals has not been adequately described. Additional data are being required.

Environmental Characteristics

Available data are insufficient to assess the environmental fate of lindane. Data gaps exist for all required studies. Preliminary adsorption data indicate that lindane has a low mobility in mineral soils and is relatively immobile in muck soils; however, the potential for lindane contamination of surface and ground water exists based on the results of a monitoring study conducted in certain southern states.

Ecological Characteristics

Avian acute oral toxicity: Data Gap
Avian dietary toxicity: 882 ppm for bobwhite quail, 561 ppm for ring-necked pheasant (moderately toxic), and >5000 ppm for mallard duck (practically nontoxic).
Freshwater fish acute (LC_{50}) toxicity: cold water species (rainbow trout) 27 ppb for technical lindane (very highly toxic), warm water species (bluegill) 68 ppb for technical lindane (very highly toxic).
Aquatic freshwater invertebrate toxicity: Daphnia 460 ppb (highly toxic). Additional data are required to fully characterize the ecological effects of lindane.
Available data are insufficient to fully assess the environmental fate of and the ecological effects from lindane.

Required Unique Labeling Summary

All manufacturing-use and end-use lindane products must bear appropriate labeling as specified in 40 CFR 162.10. In addition, the following information must appear on the labeling:

All manufacturing-use products must state that they are intended for formulation into other manufacturing-use products or end-use products only for registered uses.

All manufacturing-use products shall contain the following text in the Environmental Hazards section of the label:

"This pesticide is toxic to fish and aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or public waters unless this product is specifically identified and addressed in an NPDES permit. Do not discharge effluent containing this product into sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA."

All end-use products containing lindane that were classsified as restricted by the Final Notice of Determination concluding the RPAR shall continue to be classified for restricted use and the restricted use label must include the cancer hazard warning statement.

All end-use products shall continue to carry the applicator protection statements previously required by the Final Notice of Determination concluding the RPAR. Products with directions for foliar application to crops whose culture involves hand labor must bear the statements required under PR Notices 83-2 and 84-1 for farmworker safety, including a 24 hour re-entry interval.

End-use products with directions for spraying uninhabited buildings or empty storage bins must include protective clothing requirements, including the use of a respirator.

All end-use products for indoor use shall indicate that lindane is not to be applied to edible product areas of food processing plants or to serving areas while food is exposed.

All end-use products with uses on livestock or livestock premises must indicate not to contaminate food, feed, or water with the pesticide. Also, there must be a statement that indicates lindane is not to be applied to poultry houses, dairy barns, and milk rooms. All feed or water troughs must be covered and all livestock should be removed from animal shelters (barns, sheds, etc.) prior to treatment of the structure.

All end-use products for structural pest control must indicate that lindane is not to be applied in currently occupied areas (i.e. regular living or working areas, including finished basements or finished attics) of homes or other buildings. The characterization of a use site depends upon its intended function and not upon whether there are occupants in the area at the time of treatment.

Tolerance Assessment

The Agency is unable to complete a full tolerance assessment because the metabolism of lindane in plants and livestock animals has not been adequately described. Also, seed treatment is now considered to be a food use requiring a tolerance unless results of a radiolabeled study indicate that there is no translocation to edible parts of the plant following seed treatment. No new tolerances, except those required to support the existing seed treatment uses of lindane, will be considered until the toxicology and residue chemistry data gaps identified in the Standard have been filled.

Established tolerances are published in 40 CFR 180.133.

A listing of U.S. tolerances includes the following:

Commodity	Tolerance expressed as parts per million
Apples	1.0
Apricots	1.0
Asparagus	1.0
Avocados	1.0
Broccoli	1.0
Brussels Sprouts	1.0
Cabbage	1.0
Cattle, fat	7.0
Cauliflower	1.0
Celery	1.0
Cherries	1.0
Collards	1.0
Cucumbers	3.0
Eggplant	1.0
Goats, fat	7.0
Grapes	1.0
Guavas	1.0
Hogs, fat	4.0
Horses, fat	7.0
Kale	1.0
Kohlrabi	1.0
Lettuce	3.0
Mangoes	1.0
Melons	3.0
Mushrooms	3.0
Mustard Greens	1.0
Nectarines	1.0
Okra	1.0
Onions, dry bulb only	1.0
Peaches	1.0
Pears	1.0
Pecans	0.01
Peppers	1.0
Pineapples	1.0
Plums, incl. Prunes	1.0
Pumpkins	3.0
Quinces	1.0
Sheep, fat	7.0
Spinach	1.0
Squash	3.0
Summer Squash	3.0
Strawberries	1.0
Swiss Chard	1.0
Tomatoes	3.0

The best available data for determining an interim acceptable daily intake level of lindane is a subchronic feeding study in rats (1983) which demonstrated a No Observed Effect Level (NOEL) of 4 ppm. Based on dietary analysis, food intake, and body weight data from this particular study, the NOEL of 4 ppm is equivalent to 0.3 mg/kg/day. Using this latter value and a safety factor of 1000, the Provisional Acceptable Daily Intake (PADI) is 0.0003 mg/kg/day and the Maximum Permissible Intake (MPI) for a 60 kg person is 0.018 mg/day. The Theoretical Maximum Residue Contribution (TMRC) for lindane, based on all established tolerances, is 1.4189 mg/day/1.5 kg of diet The percent of the MPI used by the TMRC is 7883%.

Although the theoretical concentration from existing tolerances greatly exceeds the MPI, FDA market basket surveys indicate that actual residues of lindane are much lower. The Agency believes that the actual risk to consumers from the daily consumption of lindane, based on FDA market basket data for 1978-1982, is only 0.000002 mg/kg/day. Under this scenario, only 0.7% of the Maximum Permissible Intake is actually used.

4. SUMMARY OF REGULATORY POSITION AND RATIONALE

The Agency has determined that it should continue the registration of all currently registered uses of lindane. The Agency concluded in the RPAR that most uses of lindane would be continued because a risk/benefit assessment demonstrated that the benefits from the uses outweighed the risks provided certain labeling restrictions, such as restricting some uses to certified pesticide applicators, requirements for protective clothing, and label statements describing necessary precautions were added to all lindane labels. The Agency has reevaluated that decision and concludes that, except as described below, the risks and benefits are substantially the same as those described in the RPAR process.

Based on FDA market basket residue levels, which the Agency believes in this case is more generally representative of actual residues than theoretical calculations, the estimate of the upper 95% confidence level for excess cancer risk is 2×10^{-6}. The estimate of the upper 95% confidence level for excess cancer risk to applicators for various uses is estimated to be from 10^{-4} to 10^{-7}, depending upon the site and method of application. The Agency has recalculated the exposures and margins of safety for applicators for 24 use patterns and has developed initial calculations for mixer/loaders or combination mixer/loader/applicator for 3 use patterns (forestry, cucurbits, and pecans). This reassessment is based on current Agency methods and models and consideration of a lower NOEL from the subchronic rat study for uses involving subchronic type exposure.

Based on these calculations, the Agency will initiate Special Review for the forestry and uninhabited buildings and empty storage bins spray uses on the basis of risks to applicators. Use of protective clothing, including an MSHA/NIOSH approved respirator, is now being required for spraying uninhabited buildings and empty storage bins while the Special Review is underway. Protective clothing requirements stipulated in the Final Notice of Determination of the lindane RPAR will continue for all other uses. No significant changes from the exposure values presented in PD-4 occurred for twelve of the uses. The calculated exposures for cucurbits, crawl spaces, dog dusts, dog dips, shelf paper, and commercial moth sprays increased by approximately an order of magnitude, but are still acceptable. Applicator exposure data is being required for seed treatment, structural treatment, livestock spraying, dog washes, dog shampoos, and dog dusts. Air monitoring data are required for the structural treatment and dog treatment uses. Exposure studies are required, in addition to toxicity studies, to support the registrations for application of lindane to human skin/clothing by the military.

Lindane seed treatments were registered many years ago as non-food uses not requiring tolerances. The Agency now considers seed treatment to be a food use and requires data to support a tolerance unless results of a radiolabeled study indicate that there is no translocation to edible parts of the plant following seed treatment. Data from one of these two alternatives must be submitted to support the seed treatment uses. No new tolerances, except those required to support the existing seed treatment uses, will be considered until the chronic feeding and residue chemistry data gaps identified in the Standard have been filled.

Available data are insufficient to fully assess the environmental fate of lindane and its ecological effects. A full complement of such studies is being required. Precautionary label statements will continue to be required.

5. Summary of Major Data Gaps

	Due Date
- An acute inhalation study	9 months
- A 90-day inhalation study	15 months
- A dermal sensitization study	9 months
- A 21-day dermal toxicity study	12 months
- A rat chronic/oncogenicity study	50 months
- Laboratory animal blood dyscrasias study	pending
- Full complement of environmental fate studies	39 months
- Plant metabolism studies	24 months
- Livestock animal metabolism studies	18 months
- Residue chemistry studies on all crops, including seed treatment uses	48 months

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